UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/050,249	03/30/1998	HARUKI OKAMURA	OKAMURA=2B	6601

1444 7590 02/11/2002

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER
JIANG, DONG

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 02/11/2002

24

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/050,249	Applicant(s) OKAMURA ET AL.	
	Examiner Dong Jiang	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *93-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *93-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's amendment in paper No. 23, filed on 30 November 2001 is acknowledged and entered. Following the amendment, claims 93-95 and 118 are amended, and the new claim 119 is added.

Currently claims 93-119 are pending and under consideration.

Withdrawal of Objections and Rejections:

The new matter rejection of claims 93-96, 100, 104, 107-110, 113-118 under 35 U.S.C. 112, first paragraph is withdrawn in view of applicant's amendments.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 93-118 remain rejected, and claim 119 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons cited in the last Office Action, paper No. 22, mailed on 03 July 2001, at page 3.

Claim 93 remains indefinite for reciting the term "substantially the same". Applicants argument and the patent references, filed on 30 November 2001 (paper No. 23) have been fully considered, but are not deemed persuasive for reasons below.

At page 6 of the response, the applicant exemplifies that "substantially flat" is not fatally indefinite according to the Court of Appeals, and two US patents accepted the use of the claim language "substantially the same". However, the Examiner notices that the term "substantially" in the examples presented by the applicants is used to describe the degree of a physical feature ("substantially flat"), or the level of an activity (US 5,429,936, claim 11), or used in a method claim, rather than a product claim (US 6,156,315, claim 2). On the other hand, the term "substantially" in the instant claim is used to describe an amino acid sequence (part (4) of the claim). A skilled artisan would not be able to envision the detailed sequence structure of the

encompassed proteins which have "substantially the same" sequence as that described in the claim limitation. The metes and bounds of the claim, therefore, cannot be unambiguously determined. Additionally, each patent application is examined and prosecuted on its own merit, and the Examiner cannot comment on the prosecution of the other patent.

Claim 94 remains indefinite for omitting essential elements. The claim is limited by a hybridization method under specific conditions. Although the amended claim includes the washing step with 6XSSC, however, certain important wash conditions are still missing, such as washing temperature and time, which would critically effect the removal of nonspecific hybridization complexes.

The remaining claims remain rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 93, 94, 96, 118, and the dependent claims 95, 98-117 remain rejected under 35 U.S.C. 112, first paragraph, as enablement is not be commensurate in scope with the claims, for the reasons cited in the last Office Action, paper No. 22, at page 4.

Applicants argument, filed in paper No. 23 has been fully considered, but is not deemed persuasive for reasons below.

At page 7 of the response, the applicant argues that it is possible for the skilled artisan to obtain variants of SEQ ID NO:2, and to prepare monoclonal antibodies thereto without undue experimentation (the second paragraph). This argument is not persuasive because the issue is not how to make the variants and the antibodies, rather, the issue is that the antibodies to the variants would undoubtedly include those which are not specific to SEQ ID NO:2 epitopes. To the extent that the claims encompass antibodies that bind to epitopes not found in the particularly disclosed sequence, there is no written description of those epitopes. Therefore, the structural properties and use of the corresponding antibodies are not predictable. Absent a disclosed use of those antibodies non-specific to SEQ ID NO:2, the specification fails to enable the skilled artisan to make or use the full scope of the subject matter of the noted claims.

Claims 93-96 and 98-118 remain rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description for the variants of SEQ ID NO:2, for the reasons cited in the last Office Action, paper No. 22, at page 5.

Applicants argument, filed in paper No. 23 has been fully considered, but is not deemed persuasive for reasons below.

At page 8 of the response, the applicant argues that the Examiner's requirement is not a realistic one, and it is impossible to check if a monoclonal antibody to certain polypeptide binds to any other polypeptide and disclose the results in the specification (the first paragraph). This argument is not persuasive because the Examiner has not required such. The issue is that *the variants* which react with a monoclonal antibody not specifically reacting with SEQ ID NO:2 are *not described* in the specification, and therefore, it does not reasonably convey to one skilled in the relavant art that the inventors, at the time the application was filed, had possession of the claimed invention. To the extent that such variants may have epitopes not found in SEQ ID NO:2, there is no written description of such epitopes, and therefore, of antibodies that bind to them.

Claim 95 is further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the invention as now claimed. This rejection concerns the sufficiency of the written description with respect to the subject matter claimed.

The specification discloses *one* amino acid sequence with particularity, the *mouse* IL-18 with SEQ ID NO:2, and two possible isoforms differing at a single amino acid location, the residue 70 (Met^{70} and Thr^{70}), and a monoclonal antibody, mAb M-1, specific to SEQ ID NO:2. No other species of IFN-γ inducing protein, or antibodies thereof meeting the limitations of these claims were ever identified or particularly described.

The broad genus claims are represented by *one* molecular species described with particularity in the disclosure, the mouse IL-18 with SEQ ID NO:2. No other IL-18 species meeting the limitations of the claims, are identified or particularly described. The Examiner

therefore concludes that the one species of IL-18 is not likely to be representative of the genera of mammal IL-18 recited in the claim, and thus that the disclosure does not convey to those skilled in the art that the inventors were in possession of the genus of "mammal" IL-18 at the time the application was filed.

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 93-118 remain rejected, and newly submitted claim 119 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamura *et al.* (*Infect. Immun.* 61: 64-70, 1993), for the reasons cited in the last Office Action, paper No. 22, at pages 6-8.

Applicants argument, filed in paper No. 23 has been fully considered, but is not deemed persuasive for reasons below.

At page 9 of the response, the applicant argues that Nakamura's factor has a molecular weight of 50-55 kDa, loses IFN-γ inducing activity after treatment on SDS-PAGE, and the reference does not suggest the factor is a polymer of the IGIF of the claimed invention, whereas the IGIF of the present invention has a molecular weight of 19,000 + 5,000 daltons, and maintains its IFN-γ inducing activity after treatment on SDS-PAGE, therefore, it is believed that IGIF of the claimed invention and Nakamura's factor are clearly different. This argument is not

persuasive because, with respect to the issue of molecular weight difference above, a subsequent study by Okamura et al. (Infection and Immunity, 1995, 63(10):3966-72, provided by the applicants) discloses a purified murine IGIF from the liver with the same physiochemical and biological properties as the claimed IGIF, and further indicates that the same molecule was also demonstrated in the serum factor that was previously reported (by Nakamura) to have an apparent molecular mass of 75 kDa by gel filtration (and 50-55 kDa on SDS-PAGE). Moreover, Okamura demonstrates that the molecular mass of 75 kDa IGIF was reduced to 19 kDa on 0.1% SDS-PAGE in the presence of DTT, and the N-terminal amino acid sequence is the same as that of IGIF from the liver, "thus IGIF in the serum sample was proved to be the same IGIF as that found in the liver exact "(the abstract, and page 3969, the second paragraph of the left column). Therefore, the protein factor of Nakamura anticipates the invention in claims 3, and 5-6. Additionally, a later publication from the same laboratory (Ushio *et al., J. Immunol.* 156: 4274-4279, 1996, provided by the applicants) evidences that the 18-19 kDa murine factor described by in the Okamura paper has an amino acid sequence (Fig. 2) which is identical to that shown in instant SEQ ID NO: 2. In view of the similar sources and the identity of structural, biophysical, and functional properties of the instantly claimed protein and the 18-19 kDa factor described in the Okamura and Ushio papers, it reasonably appears that they are the same.

With respect to the issue of IFN-γ inducing activity of the protein after treatment on SDS-PAGE, applicants attention is directed to the difference in procedures between Nakamura's and the present invention. It is noted that a reducing agent, 2-mercaptoethanol, was used in Nakamura's SDS-PAGE procedure. Therefore, it would be expected that Nakamura's protein factor loses IFN-γ inducing activity after such treatment on SDS-PAGE. In contrast, the procedure used in the instant application is free of reducing agent (page 23, lines 12-13), therefore, the IGIF is expected to maintain its activity.

Conclusion:

No claim is allowable.

Advisory Information:

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

DJ
1/30/02